UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/147,919	03/23/99	CARDOSA M	20239-703

HM12/0605

EMILY M HALIDAY
MCCUTCHEN DOYLE BROWN & ENERSEN
THREE EMBARCADERO CENTER
SAN FRANCISCO CA 94111

EXAMINER	
MOSHER, M	
ART UNIT	**PAPER NUMBER**
1641	6

DATE MAILED: 06/05/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/147,919	Cardosa t al
Examiner	**Group Art Unit**
Mosher	1641

☒ Responsive to communication(s) filed on *3/23/99*

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *three* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *1 and 3-14* is/are pending in the applicat

Of the above, claim(s) _____ is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1 and 3-14* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *5*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

— SEE OFFICE ACTION ON THE FOLLOWING PAGES —

DETAILED ACTION

Specification

The disclosure is objected to because of the following informalities: The specification contains handwritten alterations which have not been initialed and/or dated as is required by 37 CFR 1.52(c), specifically handwritten marginal notations regarding Seq ID numbers on pages 14 and 17.

Appropriate correction is required. It is suggested that the handwritten notations be canceled and replaced with a formal amendment inserting SEQ ID numbers in the text.

Priority

This is a U.S. National application based upon PCT/EP97/05124, filed 9/23/1997. According to applicant's declaration, applicants do **NOT** claim priority to application DK 1035/96, filed 9/24/1996. Therefore the effective date for the claimed invention is 9/23/1997. A certified copy of the Danish priority document has been received from the International Bureau under PCT rule 17.2(a), but has not been considered since the oath specifically states that priority is not claimed.

Claim Rejections - 35 USC § 112

Claim 9 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 9 is drawn to a vaccine containing two components; the first component is a recombinant MVA. and the second component is a recombinant DNA vector. Since a claim

drawn to a vaccine is a claim drawn to a composition, how is the claim different from a composition containing the same two components, but used for a different purpose? While the term "vaccine" conveys an intended use, it is not clear that this intended use distinguishes the claimed composition from prior art compositions containing the same ingredients. Therefore the metes and bounds of the claimed composition are seen as indefinite.

Claims 9, 10, and 14 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. These claims are drawn to vaccine compositions and methods, which require two components, an MVA virus expressing a T7 RNA polymerase, and a second vector encoding a dengue antigen under the control of a T7 promoter. In order for the vaccine to work, the dengue antigen must be expressed in vivo. Because animal cells do not recognize a T7 promoter, the dengue antigen will not be expressed in any host cell, unless the host cell takes up both the dengue vector and the MVA virus. The specification does not teach or suggest how to deliver the virus and DNA vector to a living host, such that both components are taken up by the same cells in a manner which produces an immune response effective to treat or prevent dengue virus infection. The specification asserts that "The mode of administration, the dose and the number of administrations can be optimized by those skilled in the art in a known manner." However, at the time the invention was made, there does not appear to have been any "known manner" to deliver both of these components to the same cell in a living body. Therefore, one skilled in the art would

not have been able to use a "known manner" to administer the vaccine, and furthermore would have had reason to doubt an unsupported assertion of efficacy for the claimed vaccine. Considering the state of the art, the limited teachings in the specification, and the lack of working examples for this invention, it is concluded that undue experimentation would be required to enable the vaccine and method as claimed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 3, 5, 6, 8, and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over either Sutter et al (C2) or Altenburger (US 5,185,146), in view of Lai et al (US 5,494,671). Both Sutter et al and Altenburger teach MVA as a useful vaccinia vector for live recombinant

vaccines, having the advantage of lower virulence in humans. This differs from the claimed invention in that neither primary reference teaches Dengue DNA in the recombinant viral vaccine. However, Lai et al teaches a vaccine comprising Dengue DNA in a vaccinia vector, see for example claims 1 and 2. IT would have been within the ordinary skill in the art to combine the Dengue DNA, as taught by Lai et al, with the MVA vector as taught by Sutter et al or Altenburger, for the purpose of producing a Dengue vaccine with a less virulent vaccinia vector.

Claim 4 is rejected under 35 U.S.C. 103(a) as being unpatentable over Sutter et al (C2) or Altenburger (US 5,185,146), in view of Lai et al (US 5,494,671) as applied to claims 1, 3, 5, 6, 8, 11 above, and further in view of Sutter et al (PNAS 89:10847-10851, 1992). Claim 4 requires insertion of one or more sequences at the site of one or more naturally occurring deletions in the MVA genome. Sutter et al teaches insertion of a foreign sequence at the site of a naturally occurring deletion in MVA, and indicates that MVA has six major deletions totaling 31,000 base pairs. Therefore it would have been obvious to choose one or more of the naturally occurring deletion sites in MVA as a location for inserting one or more foreign DNAs, such as the dengue DNA.

Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over Sutter et al (C2) or Altenburger (US 5,185,146), in view of Lai et al (US 5,494,671) as applied to claims 1, 3, 5, 6, 8, 11 above, and further in view of Moss (Seminars in Immunology 2:317-327, 1990) and either or both of Hayes et al (Pediatric infectious disease journal 11(4):311-7, 1992, abstract only cited) or Bancroft.(Puerto Rico health sciences journal 6(11):23-6, 1987, abstract only cited). This claim

differs from the above in requiring the recombinant MVA to contain DNA encoding antigens of all four types of Dengue. Moss teaches that recombinant vaccinia vaccine vectors can be used as "polyvalent vaccines containing multiple genes from one microorganism or several", see page 322. Hayes et al and Bancroft teach that there are four dengue serotypes, and that severe forms of dengue may arise from sequential infection with multiple serotypes. Therefore one of ordinary skill in the art would have had motivation to vaccinate against all four dengue serotypes, and Moss provides motivation to place multiple genes in one virus. IN view of the combined teachings of the references, one of ordinary skill in the art would have been motivated to further modify the recombinant virus by use of antigens of the four different serotypes, to provide protection against all forms of the dengue virus. The invention as a whole is therefore prima facie obvious, absent unexpected results.

Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over either Sutter et al (FEBS LETT. 371:9-12, 1995) or Wyatt et al (Virology 210:202-5, 1995) in view of Lai et al (US 5,494,671). Sutter et al and Wyatt et al both teach combination of recombinant MVA expressing T7 polymerase with a plasmid containing a gene under the control of a T7 promoter, to form a system useful for efficiently expressing products in cultured cells.. The references differ from the claimed invention in that they do not use a dengue virus antigen coding sequence. However, Lai et al teaches a useful product produced by expression of a dengue coding sequence in cultured cells. It would have been within the ordinary skill of the art to choose the MVA/T7 expression system to express the dengue product. Although the references do not discuss

administration of the two components of the system to an animal, claim 9 is not directed to an administration method, but to a composition containing two components. The composition is seen as obvious, even though the references do not suggest the same use for the composition.

Claims 10 and 14 are seen as free of the art, as the prior art of record does not teach or suggest a reasonable expectation of success in treating or preventing dengue virus infection by administering a two-component T7/MVA expression system in vivo.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mary E. Mosher, Ph.D. whose telephone number is (703) 308-2926. The examiner can normally be reached on Monday -Thursday and alternate Fridays from 6:30 AM to 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's acting supervisor, James Housel, can be reached on (703) 308-4027. The fax phone number for this Group is now (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

May 30, 2000

MARY E. MOSHER
PRIMARY EXAMINER
GROUP ~~1800~~ 1600